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Applicant

BIOCOMPATIBLES UK LIMITED et al

The International Bureau transmits herewith the following documents:

☐

copy of the international application as published by the International Bureau on under
No. WO

☒

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For an explanation as to the reason for this republication of the international application, reference is made to INID codes (15), (48)
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Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **BLOCK COPOLYMERS**

(57) Abstract: Block copolymers comprise a core block formed of hydrophilic monomers and have pendant zwitterionic groups, and at least two terminal blocks, comprising stimulus-responsive groups. The core block has a degree of polymerisation of at least 100, whilst the terminal blocks have an average degree of polymerisation of at least 20. A solution of polymer in a liquid may be caused to change its characteristics, for instance rheology, upon being subjected to a stimulus such as a change in temperature or pH. Examples comprise core blocks formed of 2-methacryloyloxyethyl-2'-trimethylammonium ethylphosphate inner salt (MPC) and terminal blocks formed of 2-(diisopropylamino)ethyl methacrylate. Upon changing the pH from around 2 to around 8, an aqueous solution of the block copolymer gels, the solution becoming mobile again upon lowering the pH. The effect is due to deprotonation of a quaternary ammonium pendant ion to form a non-ionised group and subsequent protonation to form an ionised group. This changes the hydrophilicity of the terminal blocks and allowing formation of a network of micellar structures when the pendant groups are not ionised and relatively hydrophobic and associated in micelles.



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INTERNATIONAL SEARCH REPORT

International Application No
 /GB2004/000449

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C08F293/00 C08L53/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 C08F C08L C07F C09D C09J A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/28929 A (MA YINGHUA ; WILLIS SEAN LEO (GB); ARMES STEVEN PETER (GB); BIOCOMPATI) 11 April 2002 (2002-04-11) * page 17, line 6-10 ; claims 42,46,47,50,25,65,67 ; page 7, line 23-29, particularly 28-29 ; claims 43-68 ; examples 54-60,19,49-50 ; claims 1,33,34-40 ; page 4, line 4 - page 20, line 10 *	1,2,22
P,X	WO 03/074026 A (BIOCOMPATIBLES UK LTD ; LLOYD ANDREW P (GB); ARMES STEVEN PETER (GB);) 12 September 2003 (2003-09-12) * same applicant, same invention - application priority date not valid ; abstract ; claims 29-36, 1-28 ; page 12, line 12 - page 13, line 6 ; examples * ----- -/--	1,2,22, 25-28

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 03/074090 A (BIOCOMPATIBLES UK LTD ; ARMES STEVEN PETER (GB); LEWIS ANDREW LENNARD) 12 September 2003 (2003-09-12) * same applicant, same invention - application priority date not valid ; page 14, line 8-20, 26-30 ; page 12, line 18-27 ; page 23, line 8-10 ; page 4, line 16 - page 9, line 29 *	1,2,22, 25-28
X	WO 00/71660 A (RHODIA ; PROCTER & GAMBLE (US)) 30 November 2000 (2000-11-30) * claims 1,15 ; page 2, para. 3 ; page 3, para. 6 ; page 4, para. 5-7 ; page 28, para. 3 ; page 33, para. 3 - page 43, para. 3 ; claims 5,6 ; page 2, last para. - page 28, para. 1 * page 4, line 19 - page 20, line 11	1,2,22, 25-28
A	WO 01/27209 A (DAVIES MARTYN CHRISTOPHER ; CLARKE STUART (GB); BIOCOMPATIBLES LTD (GB) 19 April 2001 (2001-04-19) abstract; claims 1-20	1,2,22
A	WO 01/09208 A (REDMAN RICHARD PAUL ; BIOCOMPATIBLES LTD (GB); FREEMAN RICHARD NEIL TE) 8 February 2001 (2001-02-08) abstract; claims 1-23	1,2,22
A	US 6 395 800 B1 (JONES STEPHEN ALISTER ET AL) 28 May 2002 (2002-05-28) * claims 1-29 ; abstract *	1,2,22
A	US 5 441 841 A (LARSON JAMES R ET AL) 15 August 1995 (1995-08-15) * the whole document *	1,2,22
A	WO 01/01957 A (STRATFORD PETER WILLIAM ; TAYLOR ALISTAIR STEWART (GB); ROWAN LEE (GB)) 11 January 2001 (2001-01-11) * claims 1-16 *	1,2,22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2004/000449

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,
no additional fees are to be refunded.

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1, 2, 22, 25-28
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1,2,22

A composition comprising a solvent and a block copolymer, in which the block copolymer comprises a hydrophillic core block and at least 2 terminal blocks, each terminal block being stimulus-responsive in which the blocks are each formed at least in part by the polymerisation of ethylenically unsaturated monomers, wherein the average degree of polymerisation of each terminal block is at least 20, characterised in that the core block comprises zwitterionic pendant groups, and has a degree of polymerisation of at least 100.

For claim 2 the said block copolymer being further specified as an A-B-A structure.

2. claim: 3

A composition according to any previous claim, but in which the monomers from which the core block is formed specifically comprise compounds of the general formula, YBX...formula I, wherein Y, B, and X are as specifically detailed in application claim 3.

3. claim: 4

A composition according to claim 3 in which X is further specified as a group of the formula II as described in the lists of application claim 4.

4. claims: 5-9

A composition according to any preceding claim, but in which the monomers from which the terminal blocks are formed specifically comprise compounds of the formula VI as described in the lists of application claim 5.

5. claims: 10-15

A composition according to any preceding claim in which the monomers from which each terminal block and/or the core block is formed comprise comonomers specifically selected from compounds of the formula VII as described in the lists of application claim 10.

6. claim: 16

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A composition according to any preceding claim in which the solvent is further specified as detailed in claim 16.

7. claims: 17-20

A composition according to claim 6 in which the said substituent has a specific pH as detailed in claims 17-20.

8. claim: 21

A composition according to any preceding claim which is a gel.

9. claim: 23

A composition according to any preceding claim which comprises a biologically active agent.

10. claim: 24

A composition according to any preceding claim which comprises an imaging agent as detailed in claim 24.

11. claims: 25-28

A method in which a composition according to any claim is subjected to a stimulus to which the stimulus-responsive blocks respond as detailed in application claims 25-28.

12. claims: 29-30

A polymerisation process in which core block ethylenically unsaturated monomers comprising zwitterionic monomer are polymerised, and terminal block ethylenically unsaturated monomers are polymerised from the initiation sites on the core block, as described in application claim 29. For claim 30, the initiation sites are formed at each end of the block and not elsewhere on the core block whereby an A-B-A block copolymer is formed.

13. claim: 31

A polymerisation process according to claims 29-30, but in which the core block ethylenically unsaturated monomers comprise compounds of the formula, YBX...formula I.

14. claim: 32

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A polymerisation process according to claim 31, but in which X is further specified as a group of the formula II as described in the lists of application claim 32.

15. claims: 33-37

A polymerisation process according to any of claims 29-32, but in which specifically the terminal block ethylenically unsaturated monomers comprise compounds of the formula VI as described in the lists of application claim 33.

16. claims: 38-42

A polymerisation process according to any of claims 29-37, but in which each polymerisation step is conducted by controlled radical polymerisation, preferably by atom transfer radical polymerisation.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

/GB2004/000449

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